UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/482,788	01/13/2000	Randy m Berka	5778.200-US	7465

25907 7590 03/19/2004

NOVOZYMES BIOTECH, INC.
1445 DREW AVE
DAVIS, CA 95616

EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/482,788	BERKA ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *124-150* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *124-128,131-143,146-150* is/are rejected.

7)☒ Claim(s) *129,130,144 and 145* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 124-150 are pending.

Applicant's amendment of claims 124, 128, 131, 133, 136-139, 143, 146, 149-150 in a communication filed on 12/29/2003 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

1. Claims 143 and 150 are objected to due to the recitation of "a third nucleic acid". For clarity, it is suggested that the term be replaced with "the third nucleic acid" since the nucleic acid has been already defined in the claims from which claims 143 and 150 depend. Appropriate correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 124-127, 131-142, and 146-150 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in an Office Action mailed on 6/23/2003.

4. Applicants argue that limiting the claims to SEQ ID NO: 1 and 2 would not adequately protect the inventors since a competitor seeking to avoid infringing claims would merely have to follow the instant disclosure to find a substitute. Applicants assert that the description is sufficient to evidence

possession of the claimed invention. In particular, Applicants refer to the isolation of cyclohexadepsipeptide synthetase genes, preparation and probing of DNA libraries, methods to compare sequence identity, and characterization of cyclohexadepsipeptide synthetase activity. Applicants further argue that Applicants have shown that the polypeptide of SEQ ID NO: 2 shares approximately 59% identity with a cyclohexadepsipeptide synthetase from Fusarium scirpi and that knowledge of other Fusarium venenatum cyclohexadepsipeptide synthetase genes is not required for disruption or deletion of the gene, as evidenced by Herrmann et al. (Molecular Plant-Microbe Interactions 9:226-232, 1996; cited in previous response filed 1/28/2003). Applicants also indicate that they are not mutating a cyclohexadepsipeptide synthetase gene to change the function of the encoded enzyme but rather disrupting or deleting a portion of a cyclohexadepsipeptide synthetase gene so that no cyclohexadepsipeptide synthetase is produced. It is Applicant's contention that the previous Office Action does not provide any evidence that small structural changes can change the function of the product of a cyclohexadepsipeptide synthetase gene and that the levels of cyclohexadepsipeptide synthetase produced by the mutant Fusarium venenatum cell can be used with the method of Visconti et al. as disclosed in the specification. Applicants submit that the critical structural and functional elements required in a polynucleotide to encode a cyclohexadepsipeptide synthetase is determined by SEQ ID NO: 1 and SEQ ID NO: 2.

5. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection as it relates to claims 124-127, 131-142, and 146-150. While the Examiner acknowledges Applicants comments regarding potential infringement issues, it is noted that these issues are beyond the Examiner's control. The Examiner acknowledges (1) the teachings of the specification, (2) the teachings of Herrmann et al., (3) the fact that the claims are not directed to the mutation of a cyclohexadepsipeptide synthetase gene to change the function of the encoded enzyme, (4) the teachings of Bork, Witkowski et al., Van de Loo et al., Seffernick et al. and Broun et al. do not specifically refer to how small structural

changes in cyclohexadepsipeptide synthetase genes can change function, (5) the teachings of Visconti et al., and (6) the disclosure of SEQ ID NO: 1 and 2. However the Examiner disagrees with Applicant's contention that the specification provides adequate description of the claimed invention. The claimed invention requires the disruption or deletion of a genus of Fusarium venenatum cyclohexadepsipeptide synthetase genes. As such, one of skill in the art would require knowledge or guidance as to which is the structure of the gene to be disrupted or which elements of said genes are to be deleted to eliminate function. Furthermore, while the structure of the polynucleotide of SEQ ID NO: 1 is known, there is no teaching in the specification which indicates how the structure of the polynucleotide of SEQ ID NO: 1 correlates with the structure of any F. venenatum cyclohexadepsipeptide synthetase gene, i.e. degree of structural similarity among all F. venenatum cyclohexadepsipeptide synthetase genes. No disclosure of the critical structural elements in the polynucleotide of SEQ ID NO: 1 (or the polynucleotide used by Herrmann et al.) that correlate with cyclohexadepsipeptide synthetase function which are common to all F. venenatum cyclohexadepsipeptide synthetase genes has been presented, such that, for example, one of skill in the art would know which fragments of the polynucleotide of SEQ ID NO: 1 (or the polynucleotide used by Herrmann et al.) can be used in homologous recombination to inactivate all F. venenatum cyclohexadepsipeptide synthetase genes.

In regard to the teachings of Bork, Witkowski et al., Van de Loo et al., Seffernick et al. and Broun et al., it is noted that these references were introduced in support of the argument that assigning any function based solely on structural homology is unpredictable even when the structural similarity is high unless there is some specific known correlation between structure and function. In the instant case, this correlation is not provided neither by the art nor by the specification such that one could reasonably conclude that all F. venenatum cyclohexadepsipeptide synthetase genes will have the same structure as that of the polynucleotide of SEQ ID NO: 1 or the degree of structural variability among all F. venenatum cyclohexadepsipeptide synthetase genes.

While a sufficient written description of a genus of polynucleotides may be achieved by a recitation of a representative number of polynucleotides defined by their nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus., in the instant case, there is no structural feature which is representative of all the members of the genus of F. venenatum cyclohexadepsipeptide synthetase genes recited in the claim. Therefore, in the absence of any additional information correlating structure with cyclohexadepsipeptide synthetase function, or any correlation between the polynucleotide of SEQ ID NO: 1 and any F. venenatum cyclohexadepsipeptide synthetase gene, many structurally unrelated polynucleotides are encompassed by the genus. The specification only discloses a single species of the genus, i.e. SEQ ID NO: 1, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus of polynucleotides required to practice the claimed method. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

6. Claims 124-128, 131-143, and 146-150 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a method for producing a secreted heterologous polypeptide using a Fusarium venenatum cell, wherein the cell comprises a nucleic acid having a disruption or deletion in a cyclohexadepsipeptide synthetase gene such that said cell produces less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell, wherein said cyclohexadepsipeptide synthetase gene encodes the polypeptide of SEQ ID NO: 2, and (2) a Fusarium venenatum cell, wherein the cell comprises a nucleic acid having a disruption or deletion in a cyclohexadepsipeptide synthetase gene such that said cell produces less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell, and wherein said cyclohexadepsipeptide synthetase gene encodes the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for

(a) a method for producing a secreted heterologous protein using a mutant Fusarium venenatum cell wherein said cell comprises a nucleic acid having a disruption or deletion in any Fusarium venenatum cyclohexadepsipeptide synthetase gene such that said cell produces less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell, (b) the method of (a) wherein the cyclohexadepsipeptide synthetase gene encodes a polypeptide having 70% sequence identity to the polypeptide of SEQ ID NO: 2, or wherein said gene encodes a polypeptide encoded by a nucleic acid which hybridizes under at least medium stringency conditions with the polynucleotide of SEQ ID NO: 1, (c) any mutant Fusarium venenatum cell which has been modified to produce less cyclohexadepsipeptide synthetase than the corresponding wild type Fusarium venenatum cell by disrupting or deleting any Fusarium venenatum cyclohexadepsipeptide synthetase gene, or (d) the mutant Fusarium venenatum cell of (c) wherein the cyclohexadepsipeptide synthetase gene encodes a polypeptide having 70% sequence identity to the polypeptide of SEQ ID NO: 2, or wherein said gene encodes a polypeptide encoded by a nucleic acid which hybridizes under at least medium stringency conditions with the polynucleotide of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in an Office Action mailed on 6/23/2003.

7. Applicants submit that undue experimentation is not required to practice the claimed invention because the specification provides sufficient guidance and the skill in the art at the time of filing was high. In addition to the arguments presented regarding the written description rejection, Applicants further submit that the specification discloses how to produce a mutant cell from F. venenatum by deleting or disrupting a nucleic acid sequence encoding cyclohexadepsipeptide synthetase in the parent cell and how to express a secreted heterologous protein in said mutant cell. Applicants also assert that the specification teaches how to isolate other cyclohexadepsipeptide synthetase genes and that once the gene has been isolated and sequence, one can determine if the gene falls within the scope of the claims by

using the information provided in the specification regarding how to determine the degree of identity. According to Applicants, one can easily construct disruption or deletion vectors for transformation into any Fusarium venenatum cell, to disrupt or delete a cyclohexadepsipeptide synthetase gene without knowing the gene's sequence. Applicants assert that it is well within the skill of the art to practice the claimed invention without being provided with the corresponding DNA sequences encoding the enzymes involved in the biosynthesis of cyclohexadepsipeptide.

8. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. As indicated above regarding arguments traversing the written description rejection, the Examiner acknowledges (1) the teachings of the specification, (2) the teachings of Herrmann et al., (3) the fact that the claims are not directed to the mutation of a cyclohexadepsipeptide synthetase gene to change the function of the encoded enzyme, (4) the teachings of Bork, Witkowski et al., Van de Loo et al., Seffernick et al. and Broun et al. do not specifically refer to how small structural changes in cyclohexadepsipeptide synthetase genes can change function, (5) the teachings of Visconti et al., and (6) the disclosure of SEQ ID NO: 1 and 2. However the Examiner disagrees with Applicant's contention that the specification is enabling for the full scope of the claimed invention or that one of skill in the art can practice the claimed method without any knowledge as to the structure of cyclohexadepsipeptide synthetase genes or other genes encoding enzymes involved in the biosynthesis of cyclohexadepsipeptide. It is reiterated herein that one of skill in the art would require, at the very least, some knowledge or guidance as to how the structure of the polynucleotide of SEQ ID NO: 1 correlates with the structure of all F. venenatum cyclohexadepsipeptide synthetase genes in order to know which polynucleotide has to be inserted in a disruption or deletion vectors such that upon transformation, disruption or deletion of any F. venenatum cyclohexadepsipeptide synthetase gene would occur. As indicated above, neither the specification nor the art teaches which are the structural elements associated with cyclohexadepsipeptide synthetase function in the polynucleotide of SEQ ID NO: 1 (or the polynucleotide used by Herrmann et

al.) that are common in all F. venenatum cyclohexadepsipeptide synthetase genes. In addition, there is no disclosure of the degree of structural similarity shared among all the F. venenatum cyclohexadepsipeptide synthetase genes and the only structure disclosed, i.e. SEQ ID NO: 1. No disclosure has been provided as to the structural elements in the polynucleotide of SEQ ID NO: 1 which can be deleted, substituted or inserted to create a structural homolog encoding a polypeptide having 70% sequence identity to the polypeptide of SEQ ID NO: 2 with the same function as that of the polypeptide of SEQ ID NO: 2. Similarly, no disclosure has been provided of the structural elements in the polynucleotide of SEQ ID NO: 1 which must be present in a polynucleotide hybridizing under medium stringency conditions as recited such that it encodes a polypeptide having the same function as that of the polypeptide of SEQ ID NO: 2. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge as to the structural elements required in all F. venenatum cyclohexadepsipeptide synthetase genes and how the structure of all these genes correlate with SEQ ID NO: 1, as well as the unpredictability of the art regarding function determination based solely on structural homology, one cannot reasonably conclude that the claimed invention is fully enabled by the teachings of the specification.

Allowable Subject Matter

9. Claims 129-130 and 144-145 appear to be allowable over the prior art of record but are objected to since they depend upon a rejected claim.

Conclusion

10. Applicant's amendment of claims 124, 128, 131, 133, 136-139, 143, 146, 149-150 necessitated the new ground(s) of rejection/objections presented in this Office action. Accordingly, **THIS ACTION**

IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

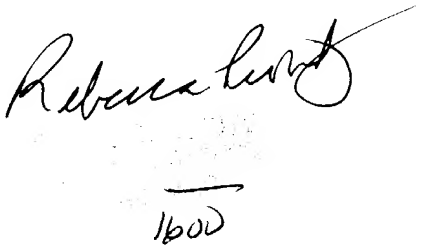
11. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 9, 2004



1600